

SEP 30 1996

Stiefel Laboratories, Inc.
Attention: William A. Carr, Jr.
Route 145
Oak Hill, NY 12460
|||||

Dear Sir:

This is in reference to your abbreviated antibiotic application dated August 31, 1994, submitted pursuant to Section 507 of the Federal Food, Drug, and Cosmetic Act for Clindets® [Clindamycin Phosphate Topical Swab (Pledgets)]; 1% (base).

Reference is also made to your amendments dated January 8, May 30 and June 6, 1996.

We have completed the review of this abbreviated application and have concluded that the drug is safe and effective for use as recommended in the submitted labeling. Accordingly, the application is approved. The Division of Bioequivalence has determined your Clindamycin Phosphate Topical Swab, 1% (base) to be bioequivalent and, therefore, therapeutically equivalent to the listed drug (Cleocin T® Topical Swab, 1% (base) of Upjohn Co.).

Under 21 CFR 314.70, certain changes in the conditions described in this abbreviated application require an approved supplemental application before the change may be made.

Post-marketing reporting requirements for this abbreviated application are set forth in 21 CFR 314.80-81. The Office of Generic Drugs should be advised of any change in the marketing status of this drug.

We request that you submit, in duplicate, any proposed advertising or promotional copy which you intend to use in your initial advertising or promotional campaigns. Please submit all proposed materials in draft or mock-up form, not final print. Submit both copies together with a copy of the proposed or final printed labeling to the Division of Drug Marketing, Advertising, and Communications (HFD-240). Please do not use Form FD-2253 (Transmittal of Advertisements and Promotional Labeling for Drugs for Human Use) for this initial submission.

We call your attention to 21 CFR 314.81(b)(3) which requires that materials for any subsequent advertising or promotional campaign be submitted to our Division of Drug Marketing, Advertising, and Communications (HFD-240) with a completed Form FD-2253 at the time of their initial use.

Sincerely yours,

Douglas L. Sporn
Director
Office of Generic Drugs
Center for Drug Evaluation and Research

Stiefel Laboratories, Inc.
Attention: William A. Carr, Jr.
Regulatory Affairs and Quality Assurance
Route 145
Oak Hill, NY 12460

OCT 11 1994

Dear Sir:

We acknowledge the receipt of your abbreviated antibiotic application submitted pursuant to Section 507 of the Federal Food, Drug and Cosmetic Act.

NAME OF DRUG: Glindamycin Phosphate Pledget, 1% (base)

DATE OF APPLICATION: August 31, 1994

DATE OF RECEIPT: September 6, 1994

We will correspond with you further after we have completed the review of your application.

Please also accompany your environmental impact analysis statement by a certification of compliance with federal, state and local environmental laws.

Although you have indicated that a third (field) copy of the application has been submitted, you have failed to certify that this copy is a "true" copy of the technical sections of the application. Refer to Sections 314.94(d)(5) and 314.440 of the Final Rule, published in the Federal Register, September 8, 1993, pages 47351 and 47352. Please provide a revised third (field) copy certification.

Clearly designate your submission of the above materials as a "New Correspondence".

Please be advised that during the AADA approval process, samples of the active and inactive ingredients, and the AADA exhibit batch(es) (which should be the same as the biobatch if a bioequivalence study was conducted) may be collected by the FDA district office staff and tested by FDA district or headquarters laboratory staff. Drug substance standards and manufacturer's documentation of the impurity profile should be made available. In addition, batch records, certificates of analysis and specifications and tests for the drug substance, drug product and inactive ingredients may be collected.

The subject product of an AADA must conform to the current official compendial monograph requirements and be compatible with the test and assay methods described in that monograph. You must submit adequate documentation and laboratory data in your AADA that prove that any non-official alternate procedures that you choose to use for the analytical control (release) of your product are equivalent to the official compendial procedures. If this information is not submitted, the review of the application will be delayed.

Please identify any communications concerning this application with the number shown above.

Should you have questions concerning this application contact:

Mark Anderson
Consumer Safety Officer
(301) 594-0360

Sincerely yours,

Gordon R. Johnston
Acting Director
Division of Labeling and Program Support
Office of Generic Drugs
Center for Drug Evaluation and Research

AADA 64-136

cc: DUP/Jacket
Division File
HFD-82
Field Copy
HFD-600/Reading File
HFD-615/MBennett
HFD-473

Endorsements: HFD-615/PRickman, Acting Chief_____date
HFD-615/KRoberts, CSO_____date
HFD-643/JHarrison, Sup. Chem._____date
WP File B:\ackaada\64136.ack
F/T by hrw 9-29-94
AADA Acknowledgement Letter!

Clindets®
(Clindamycin Phosphate Pledgets)
1%
*equivalent to 1% clindamycin
(10 mg/mL)

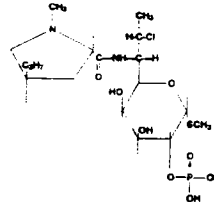


FOR EXTERNAL USE ONLY

DESCRIPTION

Clindets® (Clindamycin Phosphate Pledgets) contain clindamycin phosphate, USP at a concentration equivalent to 10 mg clindamycin per milliliter in a vehicle of isopropyl alcohol 52% v/v, propylene glycol and water. Each Clindets® pledget applicator contains approximately 1 mL of Clindamycin Phosphate Topical Solution. Clindamycin Phosphate Topical Solution has a pH range between 4.0 and 7.0.

Clindamycin phosphate is a water soluble ester of the semi-synthetic antibiotic produced by a 7(S)-chloro-substitution of the 7(R)-hydroxyl group of the parent antibiotic, lincomycin. It occurs as a white to off-white, hygroscopic, crystalline powder. It is freely soluble in water, slightly soluble in dehydrated alcohol, very slightly soluble in acetone and practically insoluble in chloroform, benzene, and ether. Clindamycin phosphate is odorless or practically odorless, and has a bitter taste. Chemically, clindamycin phosphate is $C_{18}H_{34}ClN_2O_7P$. It has the following structural formula:



The chemical name for clindamycin phosphate is Methyl 7-chloro-6,7,8-trideoxy-6-(1-methyl-2-pyrrolidinyl)-1-thio-L-threo-α-D-galacto-octopyranoside 2-(dihydrogen phosphate) (N.W. 564.97)

CLINICAL PHARMACOLOGY

Although clindamycin phosphate is inactive *in vitro*, rapid *in vivo* hydrolysis converts this compound to the antibacterially active clindamycin.

Cross resistance has been demonstrated between clindamycin and lincomycin.

Antagonism has been demonstrated between clindamycin and erythromycin.

Following multiple topical applications of clindamycin phosphate at a concentration equivalent to 10 mg clindamycin per mL in an isopropyl alcohol and water solution, very low levels of clindamycin are present in the serum (0-3 ng/mL) and less than 0.2% of the dose is recovered in urine as clindamycin.

Clindamycin activity has been demonstrated in comedones from acne patients. The mean concentration of antibiotic activity in extracted comedones after application of a Clindamycin Phosphate Pledget for 4 weeks was 597 mcg/g of comedonal material (range 0-1490). Clindamycin *in vitro* inhibits all *Propionibacterium acnes* cultures tested (MICs 0.4 mcg/mL). Free fatty acids on the skin surface have been decreased from approximately 14% to 2% following application of clindamycin.

INDICATIONS AND USAGE

Clindets are indicated in the treatment of acne vulgaris. In view of the potential for diarrhea, bloody diarrhea and pseudomembranous colitis, the physician should consider whether other agents are more appropriate. (See CONTRAINDICATIONS, WARNINGS, and ADVERSE REACTIONS.)

CONTRAINDICATIONS

Clindets are contraindicated in individuals with a history of hypersensitivity to preparations containing clindamycin or lincomycin, a history of regional enteritis or ulcerative colitis, or a history of antibiotic-associated colitis.

WARNINGS

Orally and parenterally administered clindamycin has been associated with severe colitis which may result in patient death. Use of the topical formulation of clindamycin results in absorption of the antibiotic from the skin surface. Diarrhea, bloody diarrhea, and colitis (including pseudomembranous colitis) have been reported with the use of topical and systemic clindamycin.

Studies indicate a toxin(s) produced by *Clostridia* is one primary cause of antibiotic-associated colitis. The colitis is usually characterized by severe persistent diarrhea and severe abdominal cramps and may be associated with the passage of blood and mucus. Endoscopic examination may reveal pseudomembranous colitis. Stool culture for *Clostridium difficile* and stool assay for *C. difficile* toxin may be helpful diagnostically.

When significant diarrhea occurs, the drug should be discontinued. Large bowel endoscopy should be considered to establish a definitive diagnosis in cases of severe diarrhea.



APPROVED

SEP 30 1996

Antiperistaltic agents such as opiates and diphenoxylate with atropine may prolong and/or worsen the condition. Vancomycin has been found to be effective in the treatment of antibiotic-associated pseudomembranous colitis produced by *Clostridium difficile*. The usual adult dosage is 500 mg/4 capsules to 2 grams of vancomycin orally per day in three to four divided doses administered for 7 to 10 days. Cholestyramine or colestipol resins bind to vancomycin *in vitro*. If both a resin and vancomycin are to be administered concurrently, it may be advisable to separate the time of administration of each drug.

Diarrhea, colitis, and pseudomembranous colitis have been observed to begin up to several weeks following cessation of oral and parenteral therapy with clindamycin.

PRECAUTIONS

General

Clindets contain an alcohol base which will cause burning and irritation of the eyes. In the event of accidental contact with sensitive surfaces (eye, abraded skin, mucous membranes), bathe with copious amounts of cool tap water. The solution has an unpleasant taste and caution should be exercised when applying medication around the mouth.

Clindets should be prescribed with caution in atopic individuals.

Drug Interactions

Clindamycin has been shown to have neuromuscular blocking properties that may enhance the action of other neuromuscular blocking agents. Therefore, it should be used with caution in patients receiving such agents.

Pregnancy: Teratogenic effects-Pregnancy Category B

Reproduction studies have been performed in rats and mice using subcutaneous and oral doses of clindamycin ranging from 100 to 600 mg/kg/day and have revealed no evidence of impaired fertility or harm to the fetes due to clindamycin. There are, however, no adequate and well-controlled studies in pregnant women. Because animal reproduction studies are not always predictive of human response, this drug should be used during pregnancy only if clearly needed.

Nursing Mothers

It is not known whether clindamycin is excreted in human milk following use of Clindets. However, orally and parenterally administered clindamycin has been reported to appear in breast milk. Because of the potential for serious adverse reactions in nursing infants, a decision should be made whether to discontinue nursing or to discontinue the drug, taking into account the importance of the drug to the mother.

Pediatric Use

Safety and effectiveness in the pediatric population under the age of 12 has not been established.

ADVERSE REACTIONS

In 18 clinical studies of various topical formulations of clindamycin phosphate using placebo vehicle and/or active comparator drugs as controls, patients experienced a number of treatment emergent adverse dermatological events (see table below).

Number of patients reporting events

Treatment Emergent Adverse Event	Solution n=553 (%)	Gel n=148 (%)	Lotion n=160 (%)
Bugging	62 (11)	15 (10)	17 (11)
Itching	36 (7)	15 (10)	17 (11)
Burning/itching	60 (11)	# (-)	# (-)
Dryness	105 (19)	34 (23)	29 (18)
Erythema	86 (16)	10 (7)	22 (14)
Oiliness/Oily Skin	8 (1)	26 (18)	12* (10)
Peeling	61 (11)	# (-)	11 (7)
# not recorded	* of 126 subjects		

OVERDOSAGE

Topically applied Clindamycin Phosphate formulations can be absorbed in sufficient amounts to produce systemic effects. (See WARNINGS.)

DOSEAGE AND ADMINISTRATION

Apply a thin film using a Clindets applicator for the application of Clindamycin Phosphate Topical Solution twice daily to affected area. More than one pledget may be used. Each pledget should be used only once and then discarded.

Remove pledget from foil just before use. Do not use if the seal is broken.

Discard after single use.

HOW SUPPLIED

Clindets® (Clindamycin Phosphate Pledgets) 1%** equivalent to 1% clindamycin (10 mg/mL) are available in the following sizes:

30 pledget container - NDC 0145-2472-30

48 pledget container - NDC 0145-2472-48

60 pledget container - NDC 0145-2472-60

Store at controlled room temperature, 15°-30°C (59°-86°F)

CAUTION

Federal law prohibits dispensing without prescription.

Siebel Laboratories, Inc.
Coral Gables, FL 33134

82664 Rev. 0894

Folded Envelope Size
5-3/4" x 2-1/2"



Reflex
Blue

ALL INFORMATION CONTAINED
HEREIN IS UNCLASSIFIED

SEP 30

NDC 0145-2472-03
PROFESSIONAL SAMPLE

Three Pledgets
(individually wrapped)

Clindets®
(Clindamycin Phosphate Pledgets)
1% *

*equivalent to 1% clindamycin
(10 mg/mL)

For external use only. Avoid contact with eyes.

Caution: Federal law prohibits
dispensing without prescription.



Stiefel Laboratories, Inc.
Coral Gables, FL 33134

84800 Rev. 0993

USUAL DOSAGE: See package insert for complete product information.
Store at controlled room temperature: 5° to 30°C (59° to 86°F).
Instructions for use:
1. Clean and dry the skin areas to be treated.
2. Apply a thin film of medication to the affected areas. Use sparingly, avoiding eyes and mouth.
3. If medication accidentally enters eyes, rinse thoroughly with tap water.
4. Discard pledget after single use. Do not use if the seal is broken.
The solution contains clindamycin phosphate equivalent to clindamycin 10 mg/mL.
isopropyl alcohol 52% v/v, propylene glycol, and purified water.
The solution has a pH range between 4.0 and 7.0.

Actual Size
2-3/16" x 1-13/16"



Reflex
Blue

Front

2-3/16"

NDC 0145-2472-01

One Pledget

Clindets®
(Clindamycin Phosphate Pledgets)
1% *

*equivalent to 1% clindamycin
(10 mg/mL)

For external use only.
Avoid contact with eyes.

Caution: Federal law
prohibits dispensing
without prescription.



Stiefel Laboratories, Inc.
Coral Gables, FL 33134

APPROVED
SEP 30 1996

1-13/16"

Back

2-3/16"

USUAL DOSAGE: See package insert
for complete product information.
Store at controlled room temperature
15° to 30°C (59° to 86°F).

Instructions for use:

1. Clean and dry the skin areas to be treated.
2. Apply a thin film of medication to the affected areas. Use sparingly, avoiding eyes and mouth. If medication accidentally enters eyes, rinse thoroughly with tap water.
3. Discard pledget after single use. Do not use if the seal is broken.

The solution contains clindamycin phosphate equivalent to clindamycin 10 mg/mL, isopropyl alcohol 52% v/v, propylene glycol, and purified water.
84781 Rev. 0993

1-13/16"

100%

NDC 0145-2472-01

One Pledget

Clindets®
(Clindamycin Phosphate Pledgets)
1% *

*equivalent to 1% clindamycin
(10 mg/mL)

For external use only.
Avoid contact with eyes.

Caution: Federal law
prohibits dispensing
without prescription.



Stiefel Laboratories, Inc.
Coral Gables, FL 33134

APPROVED
SEP 30 1996

USUAL DOSAGE: See package insert
for complete product information.

Store at controlled room temperature
15° to 30°C (59° to 86°F).

Instructions for use:

1. Clean and dry the skin areas to be treated.
2. Apply a thin film of medication to the affected areas. Use sparingly, avoiding eyes and mouth. If medication accidentally enters eyes, rinse thoroughly with tap water.
3. Discard pledget after single use. Do not use if the seal is broken.

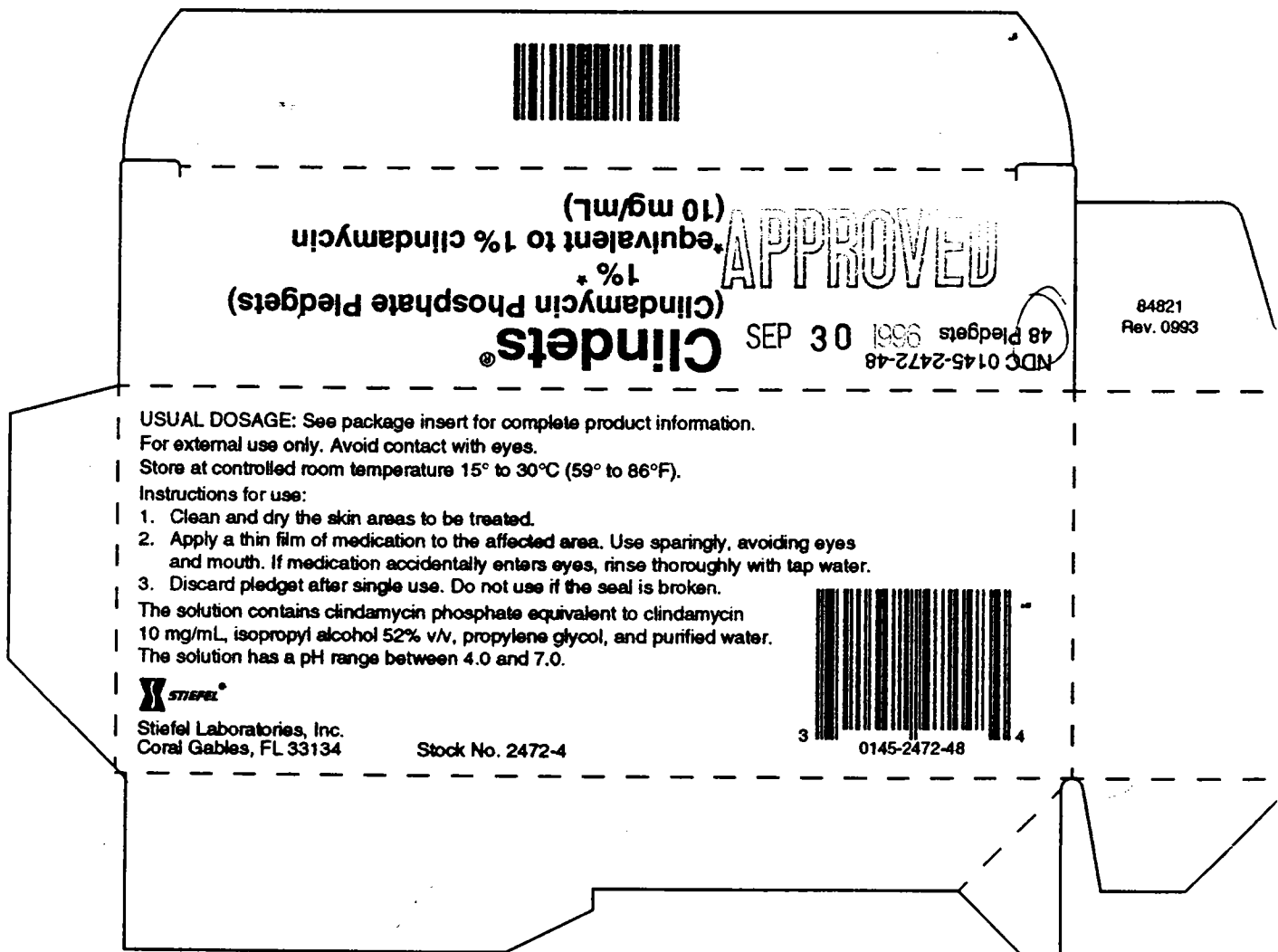
The solution contains clindamycin phosphate equivalent to clindamycin 10 mg/mL, isopropyl alcohol 52% v/v, propylene glycol, and purified water.

84781 Rev. 0993

200%

Actual Size
H: 2-1/2" x W: 1-5/16" x L: 5-1/2"

084821





Reflex
Blue

84821
Rev. 0993



NDC 0145-2472-48
48 Pledgets

Clindets®
(Clindamycin Phosphate Pledgets)
1% *

*equivalent to 1% clindamycin
(10 mg/mL)

Caution: Federal law prohibits
dispensing without prescription.

Actual Size
H: 2-1/2" x W: 1-1/8" x L: 5-1/2"

084810



APPROVED

SEP 30 1988

Clindets®
(Clindamycin Phosphate Pledgets)
1%
equivalent to 1% clindamycin
(10 mg/mL)

NDC 0145-2472-30
30 Pledgets

84810
Rev. 0993

USUAL DOSAGE: See package insert for complete product information.
For external use only. Avoid contact with eyes.
Store at controlled room temperature 15° to 30°C (59° to 86°F).

Instructions for use:

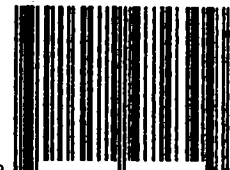
1. Clean and dry the skin areas to be treated.
2. Apply a thin film of medication to the affected area. Use sparingly, avoiding eyes and mouth. If medication accidentally enters eyes, rinse thoroughly with tap water.
3. Discard pledget after single use. Do not use if the seal is broken.

The solution contains clindamycin phosphate equivalent to clindamycin
10 mg/mL, isopropyl alcohol 52% v/v, propylene glycol, and purified water.
The solution has a pH range between 4.0 and 7.0.



Stiefel Laboratories, Inc.
Coral Gables, FL 33134

Stock No. 2472-3



3 0145-2472-30 9



Reflex
Blue

84810
Rev. 0993



NDC 0145-2472-30
30 Pledgets

Clindets[®]
(Clindamycin Phosphate Pledgets)
1% *
***equivalent to 1% clindamycin**
(10 mg/mL)

Caution: Federal law prohibits
dispensing without prescription.

Clindets®
(Clindamycin Phosphate Pledgets)
1%*
*equivalent to 1% clindamycin
(10 mg/mL)

PROFESSIONAL SAMPLE



Stiefel Laboratories, Inc.
Coral Gables, FL 33134



084851

Actual Size
H: 2-1/4" x W: 3" x L: 6-3/16"



Reflex
Blue

PROVED

SEP 30 1975

NDC C
60 Pld



NDC 0145-2472-07
60 Pledgets
(20 x 3 count pledget envelopes)



Stiefel Laboratories, Inc.
Coral Gables, FL 33134

Stock No. 2472-7

Caution: Federal law prohibits
dispensing without prescription.

Clindets®
(Clindamycin Phosphate Pl)
1% *
*equivalent to 1% clindamy
(10 mg/mL)



084851

Clindets®
 (Clindamycin Phosphate Pledgets)
 1% *
 *equivalent to 1% clindamycin
 (10 mg/mL)

APPROVED

SEP 30 1988

NDC 0145-2472-07
 60 Pledgets (20 x 3 count pledget envelopes)
 PROFESSIONAL SAMPLE

USUAL DOSAGE: See package insert for complete product information.

For external use only. Avoid contact with eyes.

Store at controlled room temperature 15° to 30°C (59° to 86°F).

Instructions for use:

1. Clean and dry the skin areas to be treated.
2. Apply a thin film of medication to the affected area.
 Use sparingly, avoiding eyes and mouth.
 If medication accidentally enters eyes, rinse thoroughly with tap water.
3. Discard pledget after single use. Do not use if the seal is broken.

The solution contains clindamycin phosphate equivalent to clindamycin 10 mg/mL, isopropyl alcohol 52% v/v, propylene glycol, and purified water.

The solution has a pH range between 4.0 and 7.0.



Stiefel Laboratories,
 Coral Gables, FL 33

84851
 Rev. 0993

Actual Size

H: 2-1/2" x W: 1-13/16" x L: 5-1/2"

084834



Clindets®
(Clindamycin Phosphate Pledgets)
1% *
equivalent to 1% clindamycin
(10 mg/mL)

NDC 0145-2472-60
60 Pledgets

84834
Rev. 0993

USUAL DOSAGE: See package insert for complete product information.

For external use only. Avoid contact with eyes.

Store at controlled room temperature 15° to 30°C (59° to 86°F).

Instructions for use:

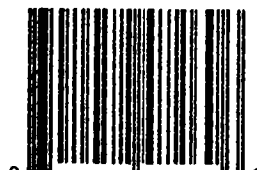
1. Clean and dry the skin areas to be treated.
2. Apply a thin film of medication to the affected area. Use sparingly, avoiding eyes and mouth. If medication accidentally enters eyes, rinse thoroughly with tap water.
3. Discard pledget after single use. Do not use if the seal is broken.

The solution contains clindamycin phosphate equivalent to clindamycin
10 mg/mL, isopropyl alcohol 52% v/v, propylene glycol, and purified water.
The solution has a pH range between 4.0 and 7.0.



Stiefel Laboratories, Inc.
Coral Gables, FL 33134

Stock No. 2472-6



3 0145-2472-60 6



Caution: F
dispensing



Reflex
Blue



NDC 0145-2472-60
60 Pledgets

APPROVED
3030

Clindets[®]
(Clindamycin Phosphate Pledgets)
1% *
*equivalent to 1% clindamycin
(10 mg/mL)

Caution: Federal law prohibits
dispensing without prescription.

1. CHEMIST'S REVIEW NO. #3

2. AADA #64-136

3. NAME AND ADDRESS OF APPLICANT

Stiefel Laboratories, Inc.
Attention: William A. Carr, Jr.
Route 145
Oak Hill, NY 12460

4. LEGAL BASIS FOR SUBMISSION

21 CFR §453.522a

Reference drug: Cleocin Phosphate® manufactured by Upjohn.
Signed certifications are provided (pp. 14-5) stating that
there are no unexpired patents and that the drug is not
subject to any exclusivity determination.

5. SUPPLEMENT(s)
N/A

6. PROPRIETARY NAME
N/A

7. NONPROPRIETARY NAME

Clindamycin Phosphate Pledget, 1% (base)

8. SUPPLEMENT(s) PROVIDE(s) FOR:
N/A

9. AMENDMENTS AND OTHER DATES:

Firm:

Original submission: 8/31/94
Amendment: 1/6/95
Amendment: 6/26/95
Amendment: 1/8/96

FDA:

Acknowledgment: 10/11/94
N/A (MAJOR) letter: 3/9/95
N/A (MINOR) letter: 12/13/95

10. PHARMACOLOGICAL CATEGORY

Antibacterial

11. Rx or OTC

Rx

12. RELATED IND/NDA/DMF(s)

13. DOSAGE FORM

Solution (Topical)

14. POTENCY

1% (as clindamycin)

15. CHEMICAL NAME AND STRUCTURE

$C_{18}H_{34}ClN_2O_8PS$ M.Wt. = 504.97

Methyl 7-chloro-6,7,8-trideoxy-6-(1-methyl-trans-4-propyl-L-2-pyrrolidinecarboxamido)-1-thio-L-threo- α -D-galacto-octopyranoside 2-(dihydrogen phosphate)

16. RECORDS AND REPORTS

N/A

17. COMMENTS

A. There is no USP monograph for Clindamycin Pledget and there is no indication from the USP Pharmacopeial Forum that there will be one. Only in the 8th supplement to the orange book 1995 the innovator's (Upjohn) pledget dosage form is added and listed as Swab; Topical. It is not listed in the following supplements.

B. The topical solution contains clindamycin phosphate, USP at a concentration equivalent to 10 mg clindamycin per mL in a vehicle of isopropyl alcohol 52% v/v, propylene glycol, and water. Each pledget applicator contains approximately 1 mL of 1% topical solution or about 10 mg clindamycin per pad.

In Amendment 1/8/96 Firm responds satisfactorily to our concerns (CR #2, 12/13/95) in order:

Q1. Regarding the specifications for the clindamycin phosphate bulk, we note that your profile and limits for the related substances are different from supplier (page 024). Please clarify.

A1. Firm claims that their specifications and limits have been set in accordance with BP which are more widely recognized and accepted, therefore more appropriate than specifications established by a single vendor. Their use of compendial (BP) specifications for clindamycin phosphate bulk would facilitate their qualification of an alternate vendor should the need arise.

Q2. It is noted from the Summary of Disposition on page 057 that when packaging lot #047308 and 047309, the amount of bulk utilized to produce

Explain.

A2. Firm explains that the set up of the (package lot #407309) material proved to be more troublesome than the (package lot #407308) material due to the the and more specifically, due to the lack of a registration mark on the pouch material which facilitates pouch cutting. As a result, variations in the cut width of the pouch material were encountered which led to excessive production waste. Firm did perform a second filling run utilizing with a registration mark (package lot #117311) and the run did perform in an entirely satisfactory manner.

Q3. In the stability data report under TAB 7, we note the potency for clindamycin declines after long-term storage at 27°C, except for lot #047309 where at the 2-yr test station the potency increases (1.03 vs. 1.00 at zero time). Please comment.

A3. Firm claims that the variation is relatively modest and may be attributable to the which has a degree of intrinsic variation. Firm promises to follow the stability of marketed product very closely and report all results to FDA for further review and comment and follow-up as appropriate.

Q4. Regarding your response for related substances specifications under TAB 8, Section A.i., we have the same concerns listed under Comment A1. Please also clarify whether the specifications provided on Page 112 and page 113 represent specifications at release and at the end of expiration date (two years), respectively.

A4. (see also under A1)
Due to the lack of compendial or other definitive data specific to related substances in finished drug product Firm developed specifications based on their analysis and review of the reference drug (Cleocin Phosphate®) as well as analysis and review of their own finished product and clindamycin phosphate bulk.

Firm's specifications provided for packaged product (at release) and for marketed product (at the end of expiration date- two years) are listed under #28 LABORATORY CONTROLS and #29 STABILITY.

18. CONCLUSIONS AND RECOMMENDATIONS

Approval recommended (pending on results of sample validation).

19. REVIEWER:

DATE COMPLETED:

Maria C. Shih

2/20/96

AADA APPROVAL SUMMARY

AADA: 64-136 **FIRM:** Stiefel Laboratories, Inc.

DRUG PRODUCT: Clindamycin Phosphate Pledget, 1% (base)

DOSAGE FORM: Topical Solution **STRENGTH:** 1%

CAMP STATEMENT/EIR UPDATE STATUS: Acceptable EER dated 2/13/96.

BIO STUDY: The waiver of in-vivo bioequivalence study was granted on 5/30/95.

METHOD VALIDATION - (DESCRIPTION OF DOSAGE FORM SAME AS FIRM'S):
Pending sample validation.

STABILITY - (ARE CONTAINERS USED IN STUDY IDENTICAL TO THOSE IN CONTAINER SECTION): The container/closure system used in the stability study was individually wrapped pledget. The pledgets incorporate a which is sealed after insertion of a saturated with Clindamycin Phosphate Topical Solution, USP. The containers used in the stability studies were identical to those described in the container section.

LABELING: FPL found satisfactory by A. Payne 1/23/96 (C. Hoppes 1/29/96).

STERILIZATION VALIDATION: N/A

SIZE OF BIO BATCH (FIRM'S SOURCE OF NDS OK?): N/A

SIZE OF STABILITY BATCHES - (IF DIFFERENT FROM BIO BATCH, WERE THEY MANUFACTURED VIA THE SAME PROCESS?):

Two bulk lots #055330 and #124303 were packaged into stability lots #047308, #047309, and #117311. The amount of product actually utilized (including waste) was approximately

, respectively.

PROPOSED PRODUCTION BATCH - (MANUFACTURING PROCESS THE SAME AS BIO/STABILITY?): The maximum batch size the firm proposes to manufacture is The manufacturing process is essentially the same as that used in manufacturing the exhibit batches.

Specifications for active ingredient: Under #23A

Specifications for the finished product: For Release see under #28; for Stability see under #29

CHEMIST: Maria C. Shih

DATE: 2/20/96

SUPERVISOR: John Harrison

DATE:

OFFICE OF GENERIC DRUGS
DIVISION OF BIOEQUIVALENCE

ANDA/AADA # 64136

SPONSOR: Sterile Labs

DRUG: Clindamycin Phosphate

DOSAGE FORM: 1% Topical Solution

STRENGTH(s): 1%

TYPE OF STUDY: Single/Multiple ~~waiver~~

Fasting/Fed

STUDY SITE:

STUDY SUMMARY:

The formulations contain Clindamycin, Isopropyl Alcohol and propylene glycol. The test product concentrations are within the acceptable range listed by the IIG.

DISSOLUTION:

N/A

PRIMARY REVIEWER:

BRANCH: I

INITIAL:

DATE: 4/7/96

BRANCH CHIEF:

BRANCH: I

INITIAL:

DATE: 4/8/96

DIRECTOR

DIVISION OF BIOEQUIVALENCE

INITIAL:

DATE: 4/8/96

DIRECTOR

OFFICE OF GENERIC DRUGS

INITIAL:

N/A

DATE:

MAY 30 1995

Clindamycin Phosphate
1% Topical Solution
~~ANDA # 64136~~
Reviewer: Andre J. Jackson
WP# 64-136W.994

Steifel Labs
Oak Hill, N.Y.
Submission Date:
September 6, 1994

Waiver Request for 1% Topical Solution

The firm is requesting a waiver of the in-vivo bioequivalence requirements for their clindamycin phosphate 1% topical solution. Clindamycin phosphate is prescribed for the treatment of acne vulgaris. The waiver request is based upon comparable formulation to the reference product Cleocin T manufactured by Upjohn.

Comments:

1. The product meets the criteria for waiver of the in-vivo bioequivalence study requirements set forth in CFR 320.22(b)(3)(i).
 - a. The test product is a solution for application to the skin.
 - b. It contains an active drug moiety in the same concentration as a drug product that is the subject of an approved full NDA.
 - c. The test product has an inactive ingredient propylene glycol which is an exception excipient in a concentration range listed within the inactive ingredients guide. The comparative formulations for the test and reference are presented in Table 1.
 - d. The test product also contains isopropyl alcohol at a concentration of which is greater than that of the reference. However, according to the interim inactive ingredients policy this deviation would be acceptable since it is within $\pm 5\%$ of the reference concentration of the isopropyl alcohol which is w/v.

Table 1. Comparative formulations for the test and reference clindamycin phosphate 1% topical solutions.

Ingredients	Cleocin T-Reference	Stiefel Labs
Clindamycin Phosphate	1 mg/100 mg	1 mg/100 mg
Isopropyl Alcohol	v/v	v/v
Propylene Glycol		

Recommendation:

1. The Division of Bioequivalence agrees that the information submitted by Stiefel Labs demonstrates that its clindomycin phosphate 1% topical solution falls under 21 CFR 320.22 b(3)(i). Therefore, the waiver of in vivo bioequivalence study requirements for clindomycin phosphate 1% topical solution is granted. The test product, clindomycin phosphate 1% topical solution is deemed bioequivalent to Cleocin 1% topical solution manufactured by Upjohn.

Andre J. Jackson
Division of Bioequivalence
Review Branch I

5/12/95

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FT INITIALLED YCH

Date: ^{30/95} 5/23/95

cc: ANDA# 64-136W-994 (original, duplicate), HFD-600 (Hare), HFD-630, HFD-658 (Huang, Jackson), Drug File, Division File

AJJ/051095/dbm/WP#64136W.994